

SEQUENCE LISTING

<110> HSC Research Development Limited Partnership et al

<120> RAS Activator Nucleic Acid Molecules, Polypeptides and Methods of Use

<130> 1786/0019

<140> PCT/CA00/00042

<141> 2000-01-20

<150> 2,259,830

<151> 1999-01-20

<160> 27

<170> PatentIn Ver. 2.1

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Phe	Met	His	Gln	Leu	Pro	Ala	Phe	Ala	Asn	Met	Thr	Met	Ser	Val	Arg
	130					135					140				
Arg	Glu	Leu	Cys	Ala	Val	Met	Val	Phe	Ala	Val	Val	Glu	Arg	Ala	Gly
145				150						155				160	
Thr	Ile	Val	Leu	Asn	Asp	Gly	Glu	Glu	Leu	Asp	Ser	Trp	Ser	Val	Ile
			165						170					175	
Leu	Asn	Gly	Ser	Val	Glu	Val	Thr	Tyr	Pro	Asp	Gly	Lys	Ala	Glu	Ile
		180						185					190		
Leu	Cys	Met	Gly	Asn	Ser	Phe	Gly	Val	Ser	Pro	Thr	Met	Asp	Lys	Glu
	195					200						205			
Tyr	Met	Lys	Gly	Val	Met	Arg	Thr	Lys	Val	Asp	Asp	Cys	Gln	Phe	Val
	210					215					220				
Cys	Ile	Ala	Gln	Gln	Asp	Tyr	Cys	Arg	Ile	Leu	Asn	Gln	Val	Glu	Lys
225				230						235				240	
Asn	Met	Gln	Lys	Val	Glu	Glu	Glu	Gly	Glu	Ile	Val	Met	Val	Lys	Glu

				245					250					255	
His	Arg	Glu	Leu	Asp	Arg	Thr	Gly	Thr	Arg	Lys	Gly	His	Ile	Val	Ile
			260					265					270		
Lys	Gly	Thr	Ser	Glu	Arg	Leu	Thr	Met	His	Leu	Val	Glu	Glu	His	Ser
		275					280					285			
Val	Val	Asp	Pro	Thr	Phe	Ile	Glu	Asp	Phe	Leu	Leu	Thr	Tyr	Arg	Thr
		290				295					300				
Phe	Leu	Ser	Ser	Pro	Met	Glu	Val	Gly	Lys	Lys	Leu	Leu	Glu	Trp	Phe
305					310					315					320
Asn	Asp	Pro	Ser	Leu	Arg	Asp	Lys	Val	Thr	Arg	Val	Val	Leu	Leu	Trp
				325					330					335	
Val	Asn	Asn	His	Phe	Asn	Asp	Phe	Glu	Gly	Asp	Pro	Ala	Met	Thr	Arg
			340					345					350		
Phe	Leu	Glu	Glu	Phe	Glu	Asn	Asn	Leu	Glu	Arg	Glu	Lys	Met	Gly	Gly
		355					360					365			
His	Leu	Arg	Leu	Leu	Asn	Ile	Ala	Cys	Ala	Ala	Lys	Ala	Lys	Arg	Arg
		370				375					380				
Leu	Met	Thr	Leu	Thr	Lys	Pro	Ser	Arg	Glu	Ala	Pro	Leu	Pro	Phe	Ile
385					390					395					400
Leu	Leu	Gly	Gly	Ser	Glu	Lys	Gly	Phe	Gly	Ile	Phe	Val	Asp	Ser	Val
				405					410					415	
Asp	Ser	Gly	Ser	Lys	Ala	Thr	Glu	Ala	Gly	Leu	Lys	Arg	Gly	Asp	Gln
			420					425					430		
Ile	Leu	Glu	Val	Asn	Gly	Gln	Asn	Phe	Glu	Asn	Ile	Gln	Leu	Ser	Lys
		435					440					445			
Ala	Met	Glu	Ile	Leu	Arg	Asn	Asn	Thr	His	Leu	Ser	Ile	Thr	Val	Lys
		450				455					460				
Thr	Asn	Leu	Phe	Val	Phe	Lys	Glu	Leu	Leu	Thr	Arg	Leu	Ser	Glu	Glu
465					470					475					480
Lys	Arg	Asn	Gly	Ala	Pro	His	Leu	Pro	Lys	Ile	Gly	Asp	Ile	Lys	Lys
				485					490					495	
Ala	Ser	Arg	Tyr	Ser	Ile	Pro	Asp	Leu	Ala	Val	Asp	Val	Glu	Gln	Val
			500					505					510		
Ile	Gly	Leu	Glu	Lys	Val	Asn	Lys	Lys	Ser	Lys	Ala	Asn	Thr	Val	Gly
		515					520					525			
Gly	Arg	Asn	Lys	Leu	Lys	Lys	Ile	Leu	Asp	Lys	Thr	Arg	Ile	Ser	Ile
		530				535					540				
Leu	Pro	Gln	Lys	Pro	Tyr	Asn	Asp	Ile	Gly	Ile	Gly	Gln	Ser	Gln	Asp
545					550					555					560
Asp	Ser	Ile	Val	Gly	Leu	Arg	Gln	Thr	Lys	His	Ile	Pro	Thr	Ala	Leu
				565					570					575	
Pro	Val	Ser	Gly	Thr	Leu	Ser	Ser	Ser	Asn	Pro	Asp	Leu	Leu	Gln	Ser
			580					585					590		
His	His	Arg	Ile	Leu	Asp	Phe	Ser	Ala	Thr	Pro	Asp	Leu	Pro	Asp	Gln
		595													

Leu Leu Arg Glu Ser Gln Ile Ser Leu Leu Gln Leu Ser Thr Val Glu
 705 710 715 720
 Val Ala Thr Gln Leu Ser Met Arg Asn Phe Glu Leu Phe Arg Asn Ile
 725 730 735
 Glu Pro Thr Glu Tyr Ile Asp Asp Leu Phe Lys Leu Arg Ser Lys Thr
 740 745 750
 Ser Cys Ala Asn Leu Lys Arg Phe Glu Glu Val Ile Asn Gln Glu Thr
 755 760 765
 Phe Trp Val Ala Ser Glu Ile Leu Arg Glu Thr Asn Gln Leu Lys Arg
 770 775 780
 Met Lys Ile Ile Lys His Phe Ile Lys Ile Ala Leu His Cys Arg Glu
 785 790 795 800
 Cys Lys Asn Phe Asn Ser Met Phe Ala Ile Ile Ser Gly Leu Asn Leu
 805 810 815
 Ala Pro Val Ala Arg Leu Arg Thr Thr Trp Glu Lys Leu Pro Asn Lys
 820 825 830
 Tyr Glu Lys Leu Phe Gln Asp Leu Gln Asp Leu Phe Asp Pro Ser Arg
 835 840 845
 Asn Met Ala Lys Tyr Arg Asn Val Leu Asn Ser Gln Asn Leu Gln Pro
 850 855 860
 Pro Ile Ile Pro Leu Phe Pro Val Ile Lys Lys Asp Leu Thr Phe Leu
 865 870 875 880
 His Glu Gly Asn Asp Ser Lys Val Asp Gly Leu Val Asn Phe Glu Lys
 885 890 895
 Leu Arg Met Ile Ala Lys Glu Ile Arg His Val Gly Arg Met Ala Ser
 900 905 910
 Val Asn Met Asp Pro Ala Leu Met Phe Arg Thr Arg Lys Lys Lys Trp
 915 920 925
 Arg Ser Leu Gly Ser Leu Ser Gln Gly Ser Thr Asn Ala Thr Val Leu
 930 935 940
 Asp Val Ala Gln Thr Gly Gly His Lys Lys Arg Val Arg Arg Ser Ser
 945 950 955 960
 Phe Leu Asn Ala Lys Lys Leu Tyr Glu Asp Ala Gln Met Ala Arg Lys
 965 970 975
 Val Lys Gln Tyr Leu Ser Asn Leu Glu Leu Glu Met Asp Glu Glu Ser
 980 985 990
 Leu Gln Thr Leu Ser Leu Gln Cys Glu Pro Ala Thr Asn Thr Leu Pro
 995 1000 1005
 Lys Asn Pro Gly Asp Lys Lys Pro Val Lys Ser Glu Thr Ser Pro Val
 1010 1015 1020
 Ala Pro Arg Ala Gly Ser Gln Gln Lys Ala Gln Ser Leu Pro Gln Pro
 1025 1030 1035 1040
 Gln Gln Gln Pro Pro Pro Ala His Lys Ile Asn Gln Gly Leu Gln Val
 1045 1050 1055
 Pro Ala Val Ser Leu Tyr Pro Ser Arg Lys Lys Val Pro Val Lys Asp
 1060 1065 1070
 Leu Pro Pro Phe Gly Ile Asn Ser Pro Gln Ala Leu Lys Lys Ile Leu
 1075 1080 1085
 Ser Leu Ser Glu Glu Gly Ser Leu Glu Arg His Lys Lys Gln Ala Glu
 1090 1095 1100
 Asp Thr Ile Ser Asn Ala Ser Ser Gln Leu Ser Ser Pro Pro Thr Ser
 1105 1110 1115 1120
 Pro Gln Ser Ser Pro Arg Lys Gly Tyr Thr Leu Ala Pro Ser Gly Thr
 1125 1130 1135
 Val Asp Asn Phe Ser Asp Ser Gly His Ser Glu Ile Ser Ser Arg Ser
 1140 1145 1150
 Ser Ile Val Ser Asn Ser Ser Phe Asp Ser Val Pro Val Ser Leu His

Asp Glu Arg Arg Gln Arg His Ser Val Ser Ile Val Glu Thr Asn Leu
 1170 1175 1180
 Gly Met Gly Arg Met Glu Arg Arg Thr Met Ile Glu Pro Asp Gln Tyr
 1185 1190 1195 1200
 Ser Leu Gly Ser Tyr Ala Pro Met Ser Glu Gly Arg Gly Leu Tyr Ala
 1205 1210 1215
 Thr Ala Thr Val Ile Ser Ser Pro Ser Thr Glu Glu Leu Ser Gln Asp
 1220 1225 1230
 Gln Gly Asp Arg Ala Ser Leu Asp Ala Ala Asp Ser Gly Arg Gly Ser
 1235 1240 1245
 Trp Thr Ser Cys Ser Ser Gly Ser His Asp Asn Ile Gln Thr Ile Gln
 1250 1255 1260
 His Gln Arg Ser Trp Glu Thr Leu Pro Phe Gly His Thr His Phe Asp
 1265 1270 1275 1280
 Tyr Ser Gly Asp Pro Ala Gly Leu Trp Ala Ser Ser Ser His Met Asp
 1285 1290 1295
 Gln Ile Met Phe Ser Asp His Ser Thr Lys Tyr Asn Arg Gln Asn Gln
 1300 1305 1310
 Ser Arg Glu Ser Leu Glu Gln Ala Gln Ser Arg Ala Ser Trp Ala Ser
 1315 1320 1325
 Ser Thr Gly Tyr Trp Gly Glu Asp Ser Glu Gly Asp Thr Gly Thr Ile
 1330 1335 1340
 Lys Arg Arg Gly Gly Lys Asp Val Ser Ile Glu Ala Glu Ser Ser Ser
 1345 1350 1355 1360
 Leu Thr Ser Val Thr Thr Glu Glu Thr Lys Pro Val Pro Met Pro Ala
 1365 1370 1375
 His Ile Ala Val Ala Ser Ser Thr Thr Lys Gly Leu Ile Ala Arg Lys
 1380 1385 1390
 Glu Gly Arg Tyr Arg Glu Pro Pro Pro Thr Pro Pro Gly Tyr Ile Gly
 1395 1400 1405
 Ile Pro Ile Thr Asp Phe Pro Glu Gly His Ser His Pro Ala Arg Lys
 1410 1415 1420
 Pro Pro Asp Tyr Asn Val Ala Leu Gln Arg Ser Arg Met Val Ala Arg
 1425 1430 1435 1440
 Ser Ser Asp Thr Ala Gly Pro Ser Ser Val Gln Gln Pro His Gly His
 1445 1450 1455
 Pro Thr Ser Ser Arg Pro Val Asn Lys Pro Gln Trp His Lys Pro Asn
 1460 1465 1470
 Glu Ser Asp Pro Arg Leu Ala Pro Tyr Gln Ser Gln Gly Phe Ser Thr
 1475 1480 1485
 Glu Glu Asp Glu Asp Glu Gln Val Ser Ala Val
 1490 1495

<210> 3
 <211> 799
 <212> DNA
 <213> Mus musculus

<400> 3
 actaaagggga acaaaagctg gagctccacc gcggtggcgg ccgctctaga actagtggat 60
 cccccggggt gcaggaattc aagcgggtggg aaggatgtct ccgctgaggc agagagcagc 120
 agcatggtgc ccgtgactac agaggaagcc aaacctgtcc ctatgcctgc ccacatagct 180
 gtgacgccga gcactaccaa gggactcatc gcacggaagg aaggcaggta ccgggagccg 240
 cctccacac ctccaggcta cgtgggcac cccattgccg atttccaga agggccttgc 300

Variable	Mean	SD	Median	Mode	Range	Skewness	Kurtosis	Shapiro-Wilk	Normality
Age	35.5	10.5	33.0	35.0	20-55	0.15	2.5	0.95	Normal
Gender	1.5	0.5	1.0	1.0	1-2	0.5	0.5	0.95	Normal
Marital Status	1.5	0.5	1.0	1.0	1-2	0.5	0.5	0.95	Normal
Education	12.5	1.5	12.0	12.0	10-15	0.1	2.0	0.95	Normal
Income	1500	500	1200	1000	500-2500	0.2	2.5	0.95	Normal
Occupation	1.5	0.5	1.0	1.0	1-2	0.5	0.5	0.95	Normal
Religion	1.5	0.5	1.0	1.0	1-2	0.5	0.5	0.95	Normal
Health Status	1.5	0.5	1.0	1.0	1-2	0.5	0.5	0.95	Normal
Stress Level	3.5	1.5	3.0	3.0	1-5	0.1	2.0	0.95	Normal
Life Satisfaction	4.5	1.0	4.0	4.0	3-5	0.1	2.0	0.95	Normal
Work-Life Balance	3.5	1.0	3.0	3.0	2-4	0.1	2.0	0.95	Normal
Family Support	4.5	1.0	4.0	4.0	3-5	0.1	2.0	0.95	Normal
Community Involvement	3.5	1.0	3.0	3.0	2-4	0.1	2.0	0.95	Normal
Personal Growth	4.5	1.0	4.0	4.0	3-5	0.1	2.0	0.95	Normal
Overall Well-being	4.5	1.0	4.0	4.0	3-5	0.1	2.0	0.95	Normal

<400>	4															
Thr	Lys	Gly	Asn	Lys	Ser	Trp	Ser	Ser	Thr	Ala	Val	Ala	Ala	Ala	Leu	
1				5					10						15	
Glu	Leu	Val	Asp	Pro	Pro	Gly	Cys	Arg	Asn	Ser	Ser	Gly	Gly	Lys	Asp	
			20				25						30			
Val	Ser	Ala	Glu	Ala	Glu	Ser	Ser	Ser	Met	Val	Pro	Val	Thr	Thr	Glu	
		35					40					45				
Glu	Ala	Lys	Pro	Val	Pro	Met	Pro	Ala	His	Ile	Ala	Val	Thr	Pro	Ser	
	50					55					60					
Thr	Thr	Lys	Gly	Leu	Ile	Ala	Arg	Lys	Glu	Gly	Arg	Tyr	Arg	Glu	Pro	
65				70						75					80	
Pro	Pro	Thr	Pro	Pro	Gly	Tyr	Val	Gly	Ile	Pro	Ile	Ala	Asp	Phe	Pro	
				85					90					95		
Glu	Gly	Pro	Cys	His	Pro	Ala	Arg	Lys	Pro	Pro	Asp	Tyr	Asn	Val	Ala	
			100					105					110			
Leu	Gln	Arg	Ser	Arg	Met	Val	Ala	Arg	Pro	Thr	Glu	Ala	Pro	Ala	Pro	
		115					120					125				
Gly	Gln	Thr	Pro	Pro	Ala	Ala	Ala	Ala	Ser	Arg	Pro	Gly	Ser	Lys	Pro	
	130					135					140					
Gln	Trp	His	Lys	Pro	Ser	Asp	Ala	Asp	Pro	Arg	Leu	Ala	Pro	Phe	Gln	
145					150					155					160	
Ala	Ala	Ser	His	Ser	Gly	Thr	Ser	Pro	Ala	Thr	Gln	Thr	His	Ala	Ser	
				165					170					175		
Arg	Pro	Ser	Arg	Gln	Ala	Ser	Gln	Glu	Arg	Arg	Arg	Thr	Lys	Met	Asn	
			180					185					190			
Lys	Cys	Leu	Leu	Phe	Glu	Ala	Gln	Ala	Pro	Xaa	Ser	Thr	Val	Ser	His	
		195					200					205				
Pro	Lys	Glu	Ser	Thr	Arg	Arg	Arg	Pro	Lys	Pro	Trp	Ser	Leu	Gly	Thr	

210	215	220
His Ile Xaa Gly Trp Trp Thr Ser Leu Pro Pro Ser Leu Pro Xaa Ser		
225	230	235 240
Ser Met Gly Leu Leu Leu Pro Phe Phe Leu Ser Pro Leu His Val Lys		
	245	250 255
Tyr Cys Glu Glu Ile Ala Leu Ala Leu Cys Arg Leu Val Ala Xaa Asn		
	260	265 270
Ala Gln Pro Ser Ser Pro Xaa Ala Ala Ala Cys His Val Thr		
	275	280 285

<210> 5
 <211> 245
 <212> PRT
 <213> Homo sapiens

<400> 5

Leu Lys Gly Thr Lys Ala Gly Ala Pro Pro Arg Trp Arg Pro Leu Xaa		
1	5	10 15
Asn Xaa Trp Ile Pro Arg Ala Ala Gly Ile Gln Ala Val Gly Arg Met		
	20	25 30
Ser Pro Leu Arg Gln Arg Ala Ala Ala Trp Cys Pro Xaa Leu Gln Arg		
	35	40 45
Lys Pro Asn Leu Ser Leu Cys Leu Pro Thr Xaa Leu Xaa Arg Arg Ala		
	50	55 60
Leu Pro Arg Asp Ser Ser His Gly Arg Lys Ala Gly Thr Gly Ser Arg		
	65	70 75 80
Leu Pro His Leu Gln Ala Thr Trp Ala Ser Pro Leu Pro Ile Ser Gln		
	85	90 95
Lys Gly Leu Ala Thr Arg Pro Gly Ser Pro Arg Ile Thr Thr Trp Pro		
	100	105 110
Cys Ser Gly Pro Ala Trp Trp His Gly Pro Leu Arg Pro Arg His Arg		
	115	120 125
Ala Arg Arg Arg Leu Gln Pro Gln Pro Ala Gly Arg Arg Leu Arg Arg		
	130	135 140
Ser Gly Gly Gly Arg Arg Xaa Thr Ser Val Cys Cys Leu Arg Arg Arg		
	145	150 155 160
Leu Leu Asp Pro Gln Xaa Ala Thr Gln Arg Arg Ala Gln Glu Asp Val		
	165	170 175
Pro Ser Leu Gly Ala Leu Ala Arg Thr Ser Glu Asp Gly Gly Pro Val		
	180	185 190

Cys Leu Leu Pro Cys Leu Lys Ala Ala Trp Gly Phe Phe Ser Pro Ser
195 200 205

Ser Phe Pro Leu Cys Met Xaa Asn Thr Val Lys Lys Leu Pro Trp His
210 215 220

Phe Ala Asp Leu Leu Leu Glu Met His Ser Pro Ala Ala Pro Glu Leu
225 230 235 240

Leu Pro Ala Thr Ser
245

<210> 6

<211> 266

<212> PRT

<213> Homo sapiens

<400> 6

Xaa Arg Glu Gln Lys Leu Glu Leu His Arg Gly Gly Gly Arg Ser Arg
1 5 10 15

Thr Ser Gly Ser Pro Gly Leu Gln Glu Phe Lys Arg Trp Glu Gly Cys
20 25 30

Leu Arg Xaa Gly Arg Glu Gln Gln His Gly Ala Arg Asp Tyr Arg Gly
35 40 45

Ser Gln Thr Cys Pro Tyr Ala Cys Pro His Ser Cys Asp Ala Glu His
50 55 60

Tyr Gln Gly Thr His Arg Thr Glu Gly Arg Gln Val Pro Gly Ala Ala
65 70 75 80

Ser His Thr Ser Arg Leu Arg Gly His Pro His Cys Arg Phe Pro Arg
85 90 95

Arg Ala Leu Pro Pro Gly Gln Glu Ala Pro Gly Leu Gln Arg Gly Pro
100 105 110

Ala Ala Val Pro His Gly Gly Thr Ala His Xaa Gly Pro Gly Thr Gly
115 120 125

Pro Asp Ala Ala Cys Ser Arg Ser Gln Pro Ala Gly Gln Gln Ala Thr
130 135 140

Val Ala Gln Ala Gln Arg Arg Arg Pro Thr Pro Arg Ala Leu Pro Gly
145 150 155 160

Ala Gly Phe Ala Gly Ala Glu Glu Asp Glu Asp Glu Gln Val Ser Ala
165 170 175

Val Xaa Gly Ala Gly Ser Leu Ile His Ser Glu Pro Pro Lys Gly Glu
180 185 190

His Lys Lys Thr Ser Gln Ala Leu Glu Pro Trp His Ala His Leu Arg
195 200 205

195	200	205
Asp Leu Leu Ser Ile Leu Glu Leu Lys Gly Gln Ser Pro Ser Asn Ala 210 215 220		
Leu Phe Ser Leu Asn Gln Met Ser Ala Ser Gln Ser Asn Ala Ala Ala 225 230 235 240		
Gly Thr Val Ile Ala Ala Asn Ala Gly Gln Ala Thr Ile Lys Arg Arg 245 250 255		
Lys Lys Ser Thr Ala Ala Pro Asn Pro Lys Lys Met Phe Glu Glu Ala 260 265 270		
Gln Met Val Arg Arg Val Lys Ala Tyr Leu Asn Ser Leu Lys Ile Leu 275 280 285		
Ser Asp Glu Asp Leu Leu His Lys Phe Ser Leu Glu Cys Glu Pro Ala 290 295 300		
His Gly Ser 305		
<210> 8		
<211> 270		
<212> PRT		
<213> Homo sapiens		
<400> 8		
Ser Ala Glu Gly Leu Asp Leu Val Ser Ala Lys Asp Leu Ala Gly Gln 1 5 10 15		
Leu Thr Asp His Asp Trp Ser Leu Phe Asn Ser Ile His Gln Val Glu 20 25 30		
Leu Ile His Tyr Val Leu Gly Pro Gln His Leu Arg Asp Val Thr Thr 35 40 45		
Ala Asn Leu Glu Arg Phe Met Arg Arg Phe Asn Glu Leu Gln Tyr Trp 50 55 60		
Val Ala Thr Glu Leu Cys Leu Cys Pro Val Pro Gly Pro Arg Ala Gln 65 70 75 80		
Leu Leu Arg Lys Phe Ile Lys Leu Ala Ala His Leu Lys Glu Gln Lys 85 90 95		
Asn Leu Asn Ser Phe Phe Ala Val Met Phe Gly Leu Ser Asn Ser Ala 100 105 110		
Ile Ser Arg Leu Ala His Thr Trp Glu Arg Leu Pro His Lys Val Arg 115 120 125		
Lys Leu Tyr Ser Ala Leu Glu Arg Leu Leu Asp Pro Ser Trp Asn His 130 135 140		

Arg Val Tyr Arg Leu Ala Leu Ala Lys Leu Ser Pro Pro Val Ile Pro
145 150 155 160

Phe Met Pro Leu Leu Leu Lys Asp Met Thr Phe Ile His Glu Gly Asn
165 170 175

His Thr Leu Val Glu Asn Leu Ile Asn Phe Glu Lys Met Arg Met Met
180 185 190

Ala Arg Ala Ala Arg Met Leu His His Cys Arg Ser His Asn Pro Val
195 200 205

Pro Leu Ser Pro Leu Arg Ser Arg Val Ser His Leu His Glu Asp Ser
210 215 220

Gln Val Ala Arg Ile Ser Thr Cys Ser Glu Gln Ser Leu Ser Thr Arg
225 230 235 240

Ser Pro Ala Ser Thr Trp Ala Tyr Val Gln Gln Leu Lys Val Ile Asp
245 250 255

Asn Gln Arg Glu Leu Ser Arg Leu Ser Arg Glu Leu Glu Pro
260 265 270

<210> 9

<211> 244

<212> PRT

<213> Mus musculus

<400> 9

Lys Ala Glu Cys Phe Glu Thr Leu Ser Ala Met Glu Leu Ala Glu Gln
1 5 10 15

Ile Thr Leu Leu Asp His Ile Val Phe Arg Ser Ile Pro Tyr Glu Glu
20 25 30

Phe Leu Gly Gln Gly Trp Met Lys Leu Asp Lys Asn Glu Arg Thr Pro
35 40 45

Tyr Ile Met Lys Thr Ser Gln His Phe Asn Glu Met Ser Asn Leu Val
50 55 60

Ala Ser Gln Ile Met Asn Tyr Ala Asp Ile Ser Ser Arg Pro Asn Ala
65 70 75 80

Ile Glu Lys Trp Val Ala Val Ala Asp Ile Cys Arg Cys Leu His Asn
85 90 95

Tyr Asn Gly Val Leu Glu Ile Thr Ser Ala Leu Asn Arg Ser Pro Ile
100 105 110

Tyr Arg Leu Lys Lys Thr Trp Ala Lys Val Ser Lys Gln Thr Lys Ala
115 120 125

Leu Met Asp Lys Leu Gln Lys Thr Val Ser Ser Glu Gly Arg Phe Lys
130 135 140

Asn Leu Arg Glu Thr Leu Lys Asn Cys Asn Pro Pro Ala Val Pro Tyr
 145 150 155 160
 Leu Gly Met Tyr Leu Thr Asp Leu Ala Phe Ile Glu Glu Gly Thr Pro
 165 170 175
 Asn Phe Thr Glu Glu Gly Leu Val Asn Phe Ser Lys Met Arg Met Ile
 180 185 190
 Ser His Ile Ile Arg Glu Ile Arg Gln Phe Gln Gln Thr Ala Tyr Arg
 195 200 205
 Ile Asp Gln Gln Pro Lys Val Ile Gln Tyr Leu Leu Asp Lys Ala Leu
 210 215 220
 Val Ile Asp Glu Asp Ser Leu Tyr Glu Leu Ser Leu Lys Ile Glu Pro
 225 230 235 240
 Arg Leu Pro Ala

<210> 10
 <211> 249
 <212> PRT
 <213> Homo sapiens

<400> 10

Asp Glu Ile Thr Leu Leu Thr Leu His Pro Leu Glu Leu Ala Arg Gln
 1 5 10 15
 Leu Thr Leu Leu Glu Phe Glu Met Tyr Lys Asn Val Lys Pro Ser Glu
 20 25 30
 Leu Val Gly Ser Pro Trp Thr Lys Lys Asp Lys Glu Val Lys Ser Pro
 35 40 45
 Asn Leu Leu Lys Ile Met Lys His Thr Thr Asn Val Thr Arg Trp Ile
 50 55 60
 Glu Lys Ser Ile Thr Glu Ala Glu Asn Tyr Glu Glu Arg Leu Ala Ile
 65 70 75 80
 Met Gln Arg Ala Ile Glu Val Met Met Val Met Leu Glu Leu Asn Asn
 85 90 95
 Phe Asn Gly Ile Leu Ser Ile Val Ala Ala Met Gly Thr Ala Ser Val
 100 105 110
 Tyr Arg Leu Arg Trp Thr Phe Gln Gly Leu Pro Glu Arg Tyr Arg Lys
 115 120 125
 Phe Leu Glu Glu Cys Arg Glu Leu Ser Asp Asp His Leu Lys Lys Tyr
 130 135 140
 Gln Glu Arg Leu Arg Ser Ile Asn Pro Pro Cys Val Pro Phe Phe Gly

Val His Leu Lys Asp Leu Ile Ser Leu Tyr Glu Ala Met Pro Asp Tyr
165 170 175

Leu Glu Asp Gly Lys Val Asn Val His Lys Leu Leu Ala Leu Tyr Asn
180 185 190

His Ile Ser Glu Leu Val Gln Leu Gln Glu Val Ala Pro Pro Leu Glu
195 200 205

Ala Asn Lys Asp Leu Val His Leu Leu Thr Leu Ser Leu Asp Leu Tyr
210 215 220

Tyr Thr Glu Asp Glu Ile Tyr Glu Leu Ser Tyr Ala Arg Glu Pro Arg
225 230 235 240

Asn His Arg

<210> 12
<211> 48
<212> PRT
<213> Unknown Organism

<220>
<223> Description of Unknown Organism: unavailable

<400> 12
Ile Arg Gly Gly Thr Lys Glu Ala Leu Ile Glu His Leu Thr Ser His
1 5 10 15

Glu Leu Val Asp Ala Ala Phe Asn Val Thr Met Leu Ile Thr Phe Arg
20 25 30

Ser Ile Leu Thr Thr Arg Glu Phe Phe Tyr Ala Leu Ile Tyr Arg Tyr
35 40 45

<210> 13
<211> 47
<212> PRT
<213> Mus musculus

<400> 13
Ile Lys Gly Gly Thr Val Val Lys Leu Ile Glu Arg Leu Thr Tyr His
1 5 10 15

Met Tyr Ala Asp Pro Asn Phe Val Arg Thr Phe Leu Thr Tyr Arg Ser
20 25 30

Phe Cys Lys Gln Glu Leu Leu Asn Leu Leu Ile Glu Arg Phe Glu
35 40 45

<210> 14
<211> 48
<212> PRT
<213> Mus musculus

<400> 14
Ile Arg Tyr Ala Ser Val Glu Ala Leu Leu Glu Arg Leu Thr Asp Leu
1 5 10 15
Arg Phe Leu Ser Ile Asp Phe Leu Asn Thr Phe Leu His Thr Tyr Arg
20 25 30
Ile Phe Thr Thr Ala Thr Val Val Leu Ala Lys Leu Ser Asp Ile Tyr
35 40 45

<210> 15
<211> 50
<212> PRT
<213> Unknown Organism

<220>
<223> Description of Unknown Organism: unavailable

<400> 15
Val Val Lys Phe Ala Ser Leu Asn Lys Leu Val Glu His Leu Thr His
1 5 10 15
Asp Ser Lys His Asp Leu Gln Phe Leu Lys Thr Phe Leu Met Thr Tyr
20 25 30
Gln Ser Phe Cys Thr Pro Glu Lys Leu Met Ser Lys Leu Gln Gln Arg
35 40 45
Tyr Xaa
50

<210> 16
<211> 77
<212> PRT
<213> Drosophila melanogaster

<400> 16
Leu Thr Arg Ser Ser Arg Asp Glu Pro Leu Asn Phe Arg Ile Val Gly
1 5 10 15
Gly Tyr Glu Leu Arg Gly Val Ala Ile Ala Thr Gly Asn Ala Ala Val
20 25 30
Gly Ile Tyr Ile Ser His Val Glu Pro Gly Ser Lys Ala Gln Asp Val
35 40 45
Gly Leu Lys Arg Gly Asp Gln Ile His Glu Val Asn Gly Gln Ser Leu

50

55

60

Asp His Val Thr Ser Lys Arg Ala Leu Glu Ile Leu Thr
 65 70 75

<210> 17

<211> 71

<212> PRT

<213> Homo sapiens

<400> 17

Asn Leu Lys Lys Asp Ala Lys Tyr Gly Leu Gly Phe Gln Ile Ile Gly
 1 5 10 15

Gly Glu Lys Met Gly Arg Leu Asp Leu Gly Ile Phe Ile Ser Ser Val
 20 25 30

Ala Pro Gly Gly Pro Ala Asp Leu Asp Gly Cys Leu Lys Pro Gly Asp
 35 40 45

Arg Leu Ile Ser Val Asn Ser Val Ser Leu Glu Gly Val Ser His His
 50 55 60

Ala Ala Ile Glu Ile Leu Gln
 65 70

<210> 18

<211> 67

<212> PRT

<213> Homo sapiens

<400> 18

Ile Val Ile His Arg Gly Ser Thr Gly Leu Gly Phe Asn Ile Val Gly
 1 5 10 15

Gly Glu Asp Gly Glu Gly Ile Phe Ile Ser Phe Ile Leu Ala Gly Gly
 20 25 30

Pro Ala Asp Leu Ser Gly Glu Leu Arg Lys Gly Asp Gln Ile Leu Ser
 35 40 45

Val Asn Gly Val Asp Leu Arg Asn Ala Ser His Glu Gln Ala Ala Ile
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Ala Leu Lys
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<210> 19

<211> 68

<212> PRT

<213> Rattus rattus

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 20 25 30
 Gly Ile Ala Asp Arg His Gly Gly Leu Lys Arg Gly Asp Gln Leu Leu
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 Ser Val Asn Gly Val Ser Val Glu Gly Glu His His Glu Lys Ala Val
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 Glu Leu Leu Lys
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 Gly Ile Asn Leu Arg Ser Ala Thr Glu Gln Gln Ala Arg Leu Ile Ile
 50 55 60
 Gly
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 <211> 98
 <212> PRT
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<400> 21
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 Gly Glu Glu Leu Asp Ser Trp Ser Val Leu Ile Asn Gly Ala Val Glu
 20 25 30
 Ile Glu His Ala Asn Gly Ser Arg Glu Glu Leu Gln Met Gly Asp Ser
 35 40 45
 Phe Gly Ile Leu Pro Thr Met Asp Lys Leu Tyr His Arg Gly Val Met
 50 55 60
 Arg Thr Lys Cys Asp Asp Cys Gln Phe Val Cys Ile Thr Gln Thr Asp
 65 70 75 80

Tyr Tyr Arg Ile Gln His Gln Gly Glu Glu Asn Thr Arg Arg His Glu
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Asp Glu

<210> 22

<211> 99

<212> PRT

<213> Homo sapiens

<400> 22

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Gly Asp Lys Gly Thr Ser Trp Tyr Ile Ile Trp Lys Gly Ser Val Asn
20 25 30

Val Val Thr His Gly Lys Gly Leu Val Thr Thr Leu His Glu Gly Asp
35 40 45

Asp Phe Gly Gln Leu Ala Leu Val Asn Asp Ala Pro Arg Ala Ala Thr
50 55 60

Ile Ile Leu Arg Glu Asp Asn Cys His Phe Leu Arg Val Asp Lys Gln
65 70 75 80

Asp Phe Asn Arg Ile Ile Lys Asp Val Glu Ala Lys Thr Met Arg Leu
85 90 95

Glu Glu His

<210> 23

<211> 97

<212> PRT

<213> Homo sapiens

<400> 23

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20 25 30

Val Tyr Val Asn Gly Glu Trp Val Thr Asn Ile Ser Glu Gly Gly Ser
35 40 45

Phe Gly Glu Leu Ala Leu Ile Tyr Gly Thr Pro Arg Ala Ala Thr Val
50 55 60

Lys Ala Lys Thr Asp Leu Lys Leu Trp Gly Ile Asp Arg Asp Ser Tyr
65 70 75 80

Arg Arg Ile Leu Met Gly Ser Thr Leu Arg Lys Arg Lys Met Tyr Glu
85 90 95

Glu

<210> 24

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<213> Homo sapiens

<400> 24

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Val Phe Gln Gly Glu Lys Leu Leu Ser Ser Ile Pro Met Trp Thr Thr
35 40 45

Phe Gly Glu Leu Ala Ile Leu Tyr Asn Cys Thr Arg Thr Ala Ser Val
50 55 60

Lys Ala Ile Thr Asn Val Lys Thr Trp Ala Leu Asp Arg Glu Val Phe
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Gln Asn Ile Met Arg Arg Thr Ala Gln Ala Arg Asp Glu Gln Tyr Arg
85 90 95

Asn

<210> 25

<211> 103

<212> PRT

<213> Mus musculus

<400> 25

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Val Leu Gly Gly Pro Asp Gly Lys Ser Val Leu Val Thr Leu Lys Ala
35 40 45

Gly Ser Val Phe Gly Glu Ile Ser Leu Leu Ala Val Gly Gly Gly Asn
50 55 60

Arg Arg Thr Ala Asn Val Val Ala His Gly Phe Thr Asn Leu Phe Ile
65 70 75 80

Leu Asp Lys Lys Asp Leu Asn Glu Ile Leu Val His Tyr Pro Glu Ser

95

Arg His Gly Glu Gly Pro Leu Leu Leu His Leu Ala Ser Pro Val Ala
65 70 75 80

1990-1991		1991-1992		1992-1993		1993-1994		1994-1995		1995-1996		1996-1997		1997-1998		1998-1999		1999-2000		2000-2001		2001-2002		2002-2003		2003-2004		2004-2005		2005-2006		2006-2007		2007-2008		2008-2009		2009-2010		2010-2011		2011-2012		2012-2013		2013-2014		2014-2015		2015-2016		2016-2017		2017-2018		2018-2019		2019-2020		2020-2021		2021-2022		2022-2023		2023-2024		2024-2025		2025-2026		2026-2027		2027-2028		2028-2029		2029-2030		2030-2031		2031-2032		2032-2033		2033-2034		2034-2035		2035-2036		2036-2037		2037-2038		2038-2039		2039-2040		2040-2041		2041-2042		2042-2043		2043-2044		2044-2045		2045-2046		2046-2047		2047-2048		2048-2049		2049-2050		2050-2051		2051-2052		2052-2053		2053-2054		2054-2055		2055-2056		2056-2057		2057-2058		2058-2059		2059-2060		2060-2061		2061-2062		2062-2063		2063-2064		2064-2065		2065-2066		2066-2067		2067-2068		2068-2069		2069-2070		2070-2071		2071-2072		2072-2073		2073-2074		2074-2075		2075-2076		2076-2077		2077-2078		2078-2079		2079-2080		2080-2081		2081-2082		2082-2083		2083-2084		2084-2085		2085-2086		2086-2087		2087-2088		2088-2089		2089-2090		2090-2091		2091-2092		2092-2093		2093-2094		2094-2095		2095-2096		2096-2097		2097-2098		2098-2099		2099-2100		2100-2101		2101-2102		2102-2103		2103-2104		2104-2105		2105-2106		2106-2107		2107-2108		2108-2109		2109-2110		2110-2111		2111-2112		2112-2113		2113-2114		2114-2115		2115-2116		2116-2117		2117-2118		2118-2119		2119-2120		2120-2121		2121-2122		2122-2123		2123-2124		2124-2125		2125-2126		2126-2127		2127-2128		2128-2129		2129-2130		2130-2131		2131-2132		2132-2133		2133-2134		2134-2135		2135-2136		2136-2137		2137-2138		2138-2139		2139-2140		2140-2141		2141-2142		2142-2143		2143-2144		2144-2145		2145-2146		2146-2147		2147-2148		2148-2149		2149-2150		2150-2151		2151-2152		2152-2153		2153-2154		2154-2155		2155-2156		2156-2157		2157-2158		2158-2159		2159-2160		2160-2161		2161-2162		2162-2163		2163-2164		2164-2165		2165-2166		2166-2167		2167-2168		2168-2169		2169-2170		2170-2171		2171-2172		2172-2173		2173-2174		2174-2175		2175-2176		2176-2177		2177-2178		2178-2179		2179-2180		2180-2181		2181-2182		2182-2183		2183-2184		2184-2185		2185-2186		2186-2187		2187-2188		2188-2189		2189-2190		2190-2191		2191-2192		2192-2193		2193-2194		2194-2195		2195-2196		2196-2197		2197-2198		2198-2199		2199-2200		2200-2201		2201-2202		2202-2203		2203-2204		2204-2205		2205-2206		2206-2207		2207-2208		2208-2209		2209-2210		2210-2211		2211-2212		2212-2213		2213-2214		2214-2215		2215-2216		2216-2217	
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Glu Glu Ala Pro Leu Ala Tyr Arg Ser His Gly Val His Thr Arg Cys
115 120 125

Gly